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EDGEWOOD ARSENAL

TECHNICAL REPORT

EATR 4054

**COLORIMETRIC DETECTION
OF ALKYL ISOCYANIDES**

by

Eleanor V. Crabtree
Edward J. Poziomek

January 1967



Physical Research Laboratory

Research Laboratories

EDGEWOOD ARSENAL

EDGEWOOD ARSENAL, MARYLAND 21010

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Defensive Research Department

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Task 1C622401A10204

Physical Research Laboratory
Research Laboratories
US ARMY EDGEWOOD ARSENAL
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FOREWORD

The work described in this report was authorized under Task 1C622401A10204, Detection and Warning Investigations (U). The experimental data are contained in notebook 7224, pp 2 to 66. This work was started in September 1964 and completed in November 1964.

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DIGEST

The subject of this research is the colorimetric detection of alkyl isocyanides. The objective was to develop a microchemical detection method for n-, sec-, and tert-butyl isocyanides.

Several aromatic amine-metal ion redox systems were investigated for the detection of alkyl isocyanides on filter paper or silica gel tubes.

It was concluded that microgram quantities of isocyanides may be easily detected on filter paper or in silica gel tubes by using benzidine acetate-cupric acetate or p, p'-tetramethyldiaminodiphenylmethane (tetrabase)-cupric sulfate reagents. Interferences include those substances that are known to interfere in the use of the same reagents for the detection of hydrogen cyanide. The lowest amount of n-, sec-, or tert-butyl isocyanide detectable is approximately 0.1 μ g.

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COLORIMETRIC DETECTION OF ALKYL ISOCYANIDES

I. INTRODUCTION.

Recent surveys of α -addition reactions¹ and synthesis methods² indicate considerable current interest in the use of isocyanides in organic chemistry. An isocyanide is usually detected by its characteristic and unpleasant odor.² Since olfaction is a sensitive and rapid method of identification, it is not surprising that only one chemical-detection method for isocyanide was found in the literature. Smith and Kalenda³ mentioned that the color test of Pertusi and Gastaldi⁴ is useful for detecting the presence of isocyanides in reaction mixtures, but gave no experimental details. This particular test is based on the oxidation of benzidine to benzidine blue by cupric acetate when a suitable complexing agent is present. It is well known for its adaptation to the detection of hydrogen cyanide.^{5, 6} We studied several aromatic amine-metal ion redox systems and will report in this paper the microchemical detection of isocyanides on filter paper or silica gel tubes by using benzidine acetate-cupric acetate or p,p'-tetramethyldiaminodiphenylmethane (tetrabase)-cupric sulfate reagents.

II. EXPERIMENTATION.

A. Benzidine Acetate-Cupric Acetate Reagent.

This reagent, which will be called the benzidine reagent in the remainder of the text, was prepared from equal volumes of (1) 2.86 gm of cupric acetate in a liter of water and (2) 675 ml of a solution of benzidine acetate (saturated at room temperature) and 525 ml of water. The solutions of cupric acetate and benzidine acetate are best stored separately in well-stoppered, dark bottles, and the reagent mixture should be freshly prepared each time it is used.

B. Tetrabase-Cupric Sulfate Reagent.

This reagent, which will be called the tetrabase reagent, was prepared by mixing equal volumes of (1) 100 mg of tetrabase and 500 mg of salicylic acid in 100 ml of acetone and (2) 1.5 gm of cupric sulfate in 100 ml of water.

C. Spot Tests on Filter Papers.

The isocyanide test was initially developed as a spot test on filter paper. Several kinds of papers were compared, since the sensitivity of certain spot tests can be increased severalfold with the proper filter paper.⁷

A detector paper [a high α -cellulose-content paper tape impregnated with about 0.8% Parex (American Cyanamid Co.) resin⁸] and several kinds of S&S (Carl Schleicher & Schuell Co., Keene, New Hampshire) and Whatman (W. and R. Bolston, Ltd., Maidstone, England) papers were used.

D. Test Apparatus for Silica Gel Tubes.

A 2- by 9-cm test tube with a capacity of about 12 ml was fitted, by means of a 19/38 standard taper joint, with an adapter supporting a side-arm air inlet and a length of glass tubing that extended to within 5 to 10 mm of the bottom of the test tube (see the figure). Silica gel tubes were connected by a short length of rubber tubing to the upper end of the glass tubing. (The use of silica gel tubes for detection is well described in the open literature, represented here by Williams and Miller,⁹ Saltzman,¹⁰ and Shepherd.¹¹) Vapors from the test tube were drawn through the detector tube by compressing a rubber bulb.

E. Techniques Involving Silica Gel Tubes.

Samples of varying amounts of the pure isocyanides dissolved in methylene chloride solution were measured with disposable microliter pipets and placed in the test apparatus described above. When an unimpregnated silica gel detector tube is used, the isocyanide vapor is collected on the silica gel, the detector tube is removed from the apparatus, and the silica gel is moistened with a drop of either reagent. The appearance of a blue color is a positive test for isocyanide. A blue color is produced directly when the isocyanide vapor is sampled onto the silica gel tubes impregnated with tetrabase reagent. These detector tubes are prepared with the following reagents impregnated in silica gel: copper sulfate pentahydrate, p,p'-tetramethyldiaminodiphenylmethane, and salicylic acid.¹² A red dye (coupled product of diazotized anthranilic acid with diethylaniline) is also added to mask the blue color of copper sulfate.

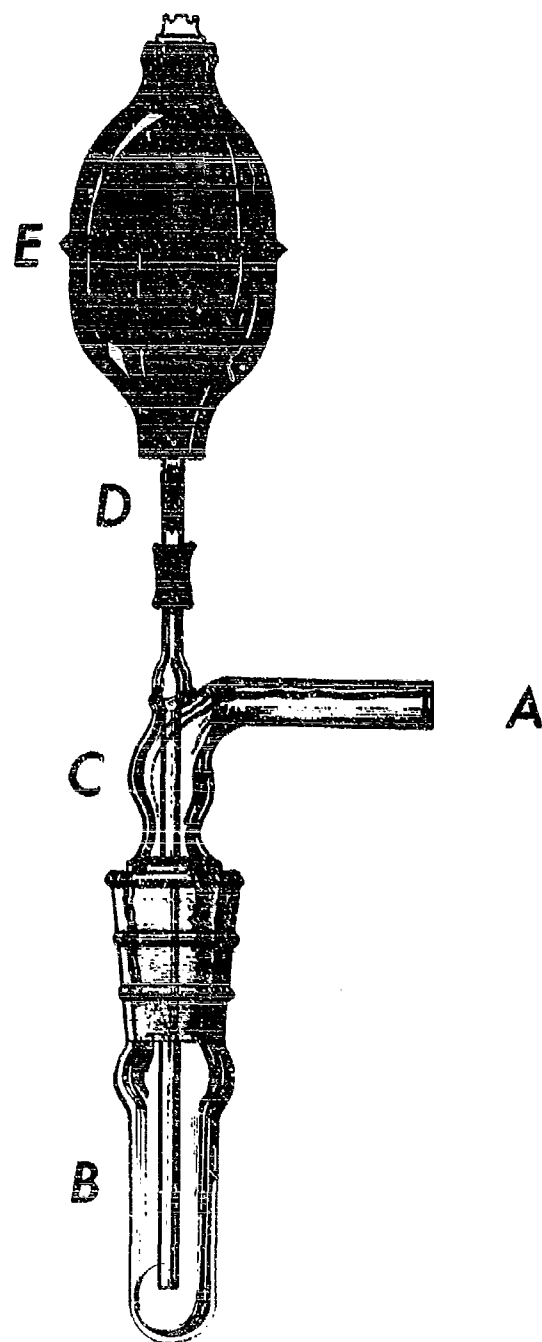


Figure. Test Apparatus for Silica Gel Tubes

(A, Air inlet; B, 2- by 9-cm test tube with 19/38 standard taper joint; C, adapter; D, silica gel tube; E, rubber aspirator bulb with one-way valve)

F. Isocyanides.

The n-, sec-, and tert-butyl isocyanides were synthesized by reacting tosyl chloride, quinoline, and the corresponding n-alkylformamide. 2, 13, 14

A typical preparation of a test solution involved: (1) weighing 77.1 mg of the chromatographically pure butyl isocyanide into a 10-ml volumetric flask and diluting to volume with methylene chloride, (2) preparing 1:50, 1:100, and 1:250 methylene chloride dilutions of the stock solution, and (3) using 1- to 50- μ l aliquots of the diluted solutions as desired for testing.

III. RESULTS.

A. Spot Tests on Filter Papers.

1. Benzidine Reagent.

In each test, 10 μ l of the benzidine reagent was placed on the filter paper, and 10 μ l of a methylene chloride solution containing 0.18 μ g of n-butyl isocyanide was added. On the basis of the intensity of the blue color produced, the papers were grouped into three categories, as follows.

Most sensitive (positive test)

Detector paper

S&S 589W

Whatman 3

Intermediately sensitive (questionable test)

Whatman 120 S&S 597

Whatman 31 S&S 604

Whatman 5

Least sensitive (negative test)

Whatman 30 S&S 576

Whatman 1 S&S 410

Whatman 4 S&S 602

Whatman 40 S&S 589 Blue ribbon

Whatman 41 S&S 589 Black ribbon

Whatman 2

2. Tetrabase Reagent.

The tetrabase reagent (10 μ l) gave a pale blue color with 5 μ g of n-butyl isocyanide on the detector paper (about the same intensity as 0.5 μ g of n-butyl isocyanide tested with the benzidine reagent). Similar results were found with the Whatman 120 paper. The blue color with tetrabase reagent was stable, whereas that with benzidine faded within a few minutes.

B. Tests in Silica Gel Tubes.

Sensitivity in isocyanide detection was improved by the use of silica gel detector tubes (see the table).

Table. Colorimetric Detection of Butyl Isocyanides in the Vapor State Using Silica Gel Tubes

Technique	Butyl isocyanides tested*		
	n-Butyl	sec-Butyl	tert-Butyl
Sampling through silica gel tubes followed by addition of benzidine reagent	0.15 μ g, definite light blue	0.09 μ g, definite test	0.12 μ g, definite test
	0.06-- 0.12 μ g, faded rapidly	0.06 μ g, faint	0.09 μ g, faint
Sampling through silica gel tubes impregnated with tetrabase reagent	0.12 μ g, definite blue color	0.09 μ g, definite test	0.09 μ g, definite test
	0.06 - 0.09 μ g, faint test	0.06 μ g, faint	0.06 μ g, faint

* The values are based on the assumption that all of the isocyanide placed in the test apparatus was sampled.

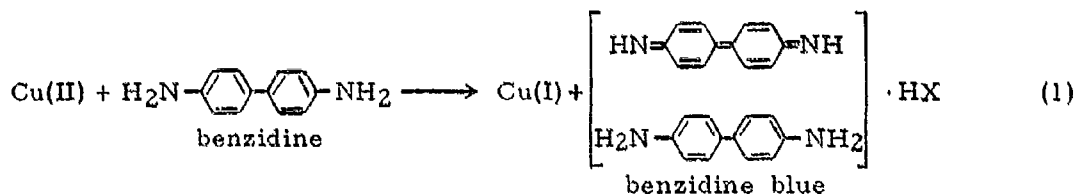
About 0.1 μ g of the butyl isocyanides was easily detected. The color formed in the benzidine test faded rapidly after 1 to 5 min. The blue color formed in tetrabase-impregnated tubes was stable; however, after prolonged standing (about 2 hr), all the impregnated tubes, including the blank controls, turned deep blue.

C. Interferences.

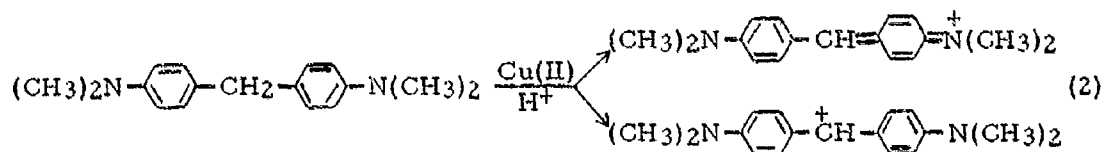
Substances that interfere in the detection of hydrogen cyanide, other than hydrogen cyanide, itself, also interfere in the detection tests for isocyanides.⁵ These include volatile oxidizing or reducing agents and certain electrophiles or acids. For example, with the tetrabase reagent, we confirmed that strong acids give a yellow color and sulfides give a brown color.

IV. DISCUSSION.

The mechanisms of the colorimetric tests for alkyl isocyanides with the benzidine or the tetrabase reagent are probably similar to those described for the well-known methods for cyanides. The benzidine test, sensitive to 0.25 μ g of cyanide in a limit of dilution of 1 in 200,000,⁵ is one of the easiest and most sensitive methods for detecting cyanide.⁶ This reaction (equation 1) takes place because the oxidation potential of Cu(II) salts is increased by the removal of Cu(I) salts through the formation of insoluble cuprous complexes.



The colored oxidation product of tetrabase contains the quinoidal or carbonium cation (equation 2). Only the salts of these cations are blue.



When they are exposed to ammonia vapors, the colorless carbinol base is formed; with the addition of acetic acid, the blue color reappears.

The benzidine test can be modified by the use of other amines, such as o-tolidine, p-diaminodiphenylamine, p-aminodimethylaniline, or o-dianisidine.

After this work had been terminated, Feigl and Anger¹⁵ published a procedure for hydrogen cyanide and cyanogen in which the benzidine and cupric acetate were replaced by tetrabase and cupric ethyl acetoacetate. The detection limit was 1 μ g of hydrogen cyanide. This reagent combination should also be effective with the alkyl isocyanides, but it was not evaluated.

Although the tests reported in the present paper are subject to interferences, they are very useful when combined with an independent measurement such as retention time in gas chromatography. Isocyanides are readily formed in the reaction of mono- N-substituted formamides with various electrophiles.² We have developed a detection method for electrophiles by combining the isocyanide test with the N-substituted formamide dehydration. Details are reported in a separate communication.*

V. CONCLUSIONS.

It was concluded that microgram quantities of isocyanides may be easily detected on filter paper or in silica gel tubes by using benzidine acetate-cupric acetate or tetrabase-cupric sulfate reagents. Interferences include those substances that are known to interfere in the use of the same reagents for the detection of hydrogen cyanide. The lowest amount of n-, sec-, or tert-butyl isocyanide detectable is approximately 0.1 μ g.

* Poziomek, E. J., Crabtree, E. V., and Hoy, D. J. Unpublished data.

LITERATURE CITED

1. Ugi, I. *Angew. Chem. Intern. Ed. Engl.* 1, 8 (1958).
2. Ugi, I., Fetzer, U., Eholzer, U., Knupper, H., and Offermann, K. *Ibid.* 4, 472 (1965).
3. Smith, P.A.S., and Kalenda, N. W. *J. Org. Chem.* 23, 1599 (1958).
4. Pertusi, C., and Gastaldi, E. *Chem. Ztg.* 37, 609 (1913).
5. Feigl, F. *Spot Tests*. Vol I, 4th ed. Elsevier Publishing Company, New York, New York. 1954.
6. Bark, L. S., and Higson, H. G. *Analyst* 88, 751 (1963).
7. Poirier, R. H., Wyant, R. E., and Harsh, Susan. *Surface Effects on Limits of Visual Detection of Chromophoric Substances*. In: *Conference on Surface Effects in Detection*. Bregman, J. I., and Dravnieks, A., eds. Spartan Books, Inc., Washington, D. C. 1965.
8. Military Specification. MIL-P-51181 (M7). *Detector Paper*. US Government Printing Office. 4 March 1966.
9. Williams, D. D., and Miller, R. R. *Anal. Chem.* 34, 225 (1962).
10. Saltzman, B. E. *Am. Ind. Hyg. Assoc. J.* 23, 112 (1962).
11. Shepherd, M. *Anal. Chem.* 19, 77 (1947).
12. Military Specification. MIL-S-50021A. *Silica Gel, Impregnated; For Hydrogen Cyanide (AC) Detector Tubes*. US Government Printing Office. 29 August 1960.
13. Casanova, J., Jr., Schuster, R. E., and Jerner, N. D. *J. Chem. Soc.* 4280 (1963).
14. Hoy, D. J., and Poziomek, E. J. CRDLR 3325. *Isocyanide Synthesis*. December 1965. UNCLASSIFIED Report.
15. Feigl, F., and Anger, V. *Analyst* 91, 280 (1966).

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Security Classification

DOCUMENT CONTROL DATA - R&D																
(Security classification of title, body of abstract and indexing annotation must be entered when the overall report is classified)																
1. ORIGINATING ACTIVITY (Corporate author) US Army Edgewood Arsenal ATTN: SMUEA-RPRE Edgewood Arsenal, Maryland 21010		2a. REPORT SECURITY CLASSIFICATION UNCLASSIFIED 2b. GROUP N/A														
3. REPORT TITLE COLORIMETRIC DETECTION OF ALKYL ISOCYANIDES																
4. DESCRIPTIVE NOTES (Type of report and inclusive dates) This work was started in September 1964 and completed in November 1964.																
5. AUTHOR(S) (Last name, first name, initial) Crabtree, Eleanor V., and Poziomek, Edward J.																
6. REPORT DATE January 1967	7a. TOTAL NO. OF PAGES 31	7b. NO. OF REFS 15														
8a. CONTRACT OR GRANT NO. b. PROJECT NO. c. Task No. 1C622401A10204 d.	9a. ORIGINATOR'S REPORT NUMBER(S) EATR 4054 9b. OTHER REPORT NO(S) (Any other numbers that may be assigned this report) N/A															
10. AVAILABILITY/LIMITATION NOTES This document is subject to special export controls and each transmittal to foreign governments or foreign nationals may be made only with prior approval of the Commanding Officer, US Army Edgewood Arsenal, ATTN: SMUEA-TSTI-T, Edgewood Arsenal, Maryland 21010.																
11. SUPPLEMENTARY NOTES Detection and warning investigations	12. SPONSORING MILITARY ACTIVITY N/A															
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14. KEYWORDS <table border="0"><tr><td>Isocyanides</td><td>Tosyl chloride</td></tr><tr><td>Isonitriles</td><td>Cyanides</td></tr><tr><td>Benzidine-Cu(II) reagent</td><td>Silica gel tubes</td></tr><tr><td>Tetrabase-Cu(II) reagent</td><td>Spot tests</td></tr><tr><td>Detection</td><td>Colorimetry</td></tr><tr><td>Electrophiles</td><td>Butyl isocyanides</td></tr><tr><td>Alkylformamides</td><td></td></tr></table>			Isocyanides	Tosyl chloride	Isonitriles	Cyanides	Benzidine-Cu(II) reagent	Silica gel tubes	Tetrabase-Cu(II) reagent	Spot tests	Detection	Colorimetry	Electrophiles	Butyl isocyanides	Alkylformamides	
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